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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,787	09/26/2001	Preeti Lal	PF-0356-3 DIV	5251

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EXAMINER
SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
1652	12

DATE MAILED: 09/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,787	LAL ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3 Sep 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-14 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-14,21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed September 3, 2002 amending claim 14 and adding claim 21 has been entered.

The Declaration under 37 CFR 1.132 of Dr. Preeti Lal filed September 3, 2002 has been entered.

Claims 2-14 and 21 are pending.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2-14 and 21 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility, credible asserted utility or a well established utility.

Applicants disclose a nucleic acid sequences (SEQ ID NO: 68) encoding the amino acid sequence of SEQ ID NO: 19 (HRM-19). The specification teaches that SEQ ID NO:19 that is 351 amino acids in length and has one potential mitochondrial motif, P_{31}LDVVKVRL. It further discloses that HRM-19 has sequence homology with C. *elegans* C16C10 (g577542) and is found in cDNA libraries associated with cell proliferation, cancer and immune response (page 18, lines 24-28). The specification

describes generic functions for the protein and the nucleic acid encoding thereof. The utility of the nucleic acid is said to be used in a method to detect expression of a nucleic acid in a sample and to recombinantly make the polypeptide of SEQ ID NO: 19 which neither the gene nor the polypeptide are associated with a specific use. The specification does not assert any specific utility for HRM-19 and provides no additional evidence that HRM-19 has any specific function. The sequence search performed by PTO shows that SEQ ID NO:19 has about 35% homology with a C. *elegans* putative mitochondrial carrier C16C10. It is nearly impossible from sequence homology alone to attribute a specific and substantial function for the protein. There is no additional data to support any specific function. Such data would include the number of the specific domains associated with said function, and location of highly conserved charge-pairs, for example. Even accepting the plausible utility of HRM-19 being a mitochondrial carrier, one of ordinary skill in the art would not know which compound is a substrate for the carrier. Humans produce many mitochondrial carriers and each mitochondrial carrier is expected to have a specific substrate(s) and function. The art teaches that there are many mitochondrial carriers that import various metabolites, nucleotides, cofactors and compounds which are not synthesized in mitochondria. They have several repetitive elements in the primary structure (Palmieri, pages 48 and 49). Therefore, as disclosed, a protein of SEQ ID NO:19 is an uncharacterized protein with no known function.

Furthermore, for a method of detection of a nucleic acid in a sample to be useful, one must know the biological significance of the polypeptide(s) which is(are) being detected. Without this information, the results of the expression profile are useless because one would not know if the polypeptide expression should be increased or decreased or even what significance could be attributed to such changes in expression profiles. Without this knowledge, which could not be gleaned from the instant specification as filed, one of ordinary skill in the art at the time the instant invention was made would not have been able to use the information obtained from an expression profile in a useful manner. There is no evidence to the contrary.

Claims 13, 21 and 14 are drawn to a method for diagnosing an unspecified disease and lung cancer, respectively.

Neither the specification nor the art of record disclose any specific disease or conditions that can be diagnosed using a DNA encoding SEQ ID NO:19.There is no indication that increasing or decreasing the expression of HRM-19 would have any use in diagnosing any diseases. Therefore, diagnosing of an unspecified, undisclosed disease or condition or cancer or immune response would require or constitute carrying out further research to identify or reasonably confirm a disease that can be diagnosed using a DNA encoding SEQ ID NO:19. With regard to diagnosis of disease, in order for a polynucleotide to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed

polypeptide and a disease or disorder. The presence of a polypeptide/polynucleotide in tissue that is derived from some cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed polypeptide and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polynucleotide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in a specific diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed polynucleotide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide and any disease or disorder and the lack of any correlation between the claimed polynucleotide with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself.

Therefore, it appears that the main utility of the polypeptide and nucleic acid is to carry out further research to identify the biological function and possible diseases associated with said function. Substantial utility defines a "real world" use. Utilities

that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utility. In view of the above, a DNA encoding SEQ ID NO:19 and methods of use thereof have no specific, substantial, credible and well-established utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-14 and 21 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to Arguments

Applicant's arguments filed September 3, 2002 have been fully considered but they are not persuasive.

Applicants argue that Declaration of Dr. Lal support the utility for HRM-19 as a mitochondrial carrier protein asserted in the specification (Remarks, page 3). This is

not agreed with because what is asserted in the specification is that HRM-19 "has one potential mitochondrial carrier motif ... [and] has sequence homology with C. elegans C16C10 (g577542) and is found in cDNA libraries associated with cell proliferation, cancer and immune response" (specification, page 18, lines 24-28). The sequence search performed by PTO shows that SEQ ID NO:19 has about 35% homology with a C. *elegans* putative mitochondrial carrier C16C10. In most cases, such degree of homology does not allow the prediction of specific function. As evident from the above description of HRM-19, the specification did not assert that HRM-19 is a mitochondrial carrier protein but only that it has "one potential mitochondrial motif" (specification, page 18, lines 26-27). The presence of "one potential mitochondrial motif" does not necessarily render the protein a mitochondrial carrier. Further, C. elegans C16C10 is only a putative mitochondrial carrier protein. Therefore, the specific utility was not asserted at the time of filing. Furthermore, even if the protein belongs to a family of proteins, its specific function is still uncharacterized and, in the instant case, is unanticipated. In fact, the reference of Yu et al., cited in the Declaration, describes CGI-69, which is HRM-19 with substitution F239L, as a previously uncharacterized protein(abstract). Yu et al. elucidate its properties that are different from of other mitochondrial carrier proteins. They teach that CGI-69 is different from other mitochondrial carriers as lacking uncoupling ability (page 372). The properties discussed by Yu et al. are not described by the specification. Therefore, Yu et al.

reference can not provide support for the HRM-19 function that was not described in the specification and for utility that was not asserted in the specification at the time the application was filed.

Applicants argue with the support of the Declaration that the gene encoding SEQ ID NO:19 is up-regulated in lung cancer (Remarks, page 5; Declaration, Exhibit D). Regardless of whether these data can provide the support for the utility, said utility is not described in the specification, i.e., there is no mentioning that the gene encoding SEQ ID NO:19 is up-regulated in lung cancer. The specification provides no specific teaching regarding HRM-19 but only the teaching regarding all HRM in general. It teaches that "polynucleotides encoding HRM may be used for the diagnosis" of various diseases of a non-discriminatory list of all human organs (emphasis added, specification, page 47, line 24 through page 48, line 24). Nowhere the specification discloses that the gene encoding SEQ ID NO:19 is up-regulated in lung cancer. Therefore, the utility for the gene encoding SEQ ID NO:19 was not specifically asserted in the specification at the time of filing.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP §

706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
September 11, 2002